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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,130	02/04/1999	BERNARD DUJON	3495.0111-10	3378

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	26

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/244,130	Applicant(s) DUJON ET AL.	
	Examiner Sumesh Kaushal Ph.D.	Art Unit 1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05/30/02 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *28 June 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): *See Continuation Sheet*.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *53-86*.

Claim(s) withdrawn from consideration: *none*.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 3. Applicant's reply has overcome the following rejection(s): Cancelation of claims 48-52 and 87-93 has over come rejection under 35 USC 112(1) regarding enablement and written description issues.

Continuation of 5. does NOT place the application in condition for allowance because

Double Patenting

Claims 53-57 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 15, 28, 29, 30, 32 of co-pending Application No.08/643732 (Now US Patent No. 6395959) for the same reasons of record as set forth in the official action mailed on 12/31/01.

Claim Rejections - 35 USC § 112

Claims 53-86 stand rejected under 35 U.S.C. 112, first paragraph regarding **written description issues**, for the same reasons of record as set forth in the official action mailed on 12/31/01. The applicant further argues that mere presence of Group-I endonuclease recognition site is all that is required of applicant's transgenic mice comprising a Group-I endonuclease recognition site. The applicant argues that Dr. Choulika's declaration sates that a mouse comprising Group-I endonuclease recognition site should have same wild-type phenotype as a mouse containing I-SceI site. The applicant argues that the chimeric mice as disclosed by Dr. Choulika's declaration are transgenic mice. The applicant argues that transgenic mice only need to carry exogenous DNA to be transgenic but that DNA need not to be germ line transmissible (response, page 3, para.2). The applicant concluded that D3 ES cells are routinely used to make transgenic mice and in view of that Dr. Choulika's declaration (second) one would have reasonable expectation of success to obtain germ line transmission.

The applicant's argument has been addressed in the earlier office action which clearly sates that few disclosed embodiments are not representative of the products claimed. The invention as claimed encompasses any and all endonucleases sites selected from Group-I-intron-encoded endonuclease sites. At best the specification only discloses endonucleases sites for Class I (I-SceI, I-SceIV, I-PanI) and Class II (I-TevI). The specification fails to disclose any endonuclease sites that represent Class III (I-PpoI), Class IV (I-TevII) and Class V (I-TevIII) endonucleases sites (spec. page 27 and fig-6). In addition, the instant specification discloses that Class III, IV and V endonuclease sites are not represented by any typical structural motifs (spec. page 27, lines 13-21). The specification fails to disclose any consensus nucleotide sequences and/or structural motifs that represent a particular Class of Group-I encoded endonuclease sites that exist in nature. In addition, the specification only discloses transgenic yeast or transformed/transfected mouse cell lines (NIH3T3, PCC7-s). Considering the unpredictability in the making of a transgnic mice Dr. Choulika's declaration even fails to disclose a single transgenic mouse that encodes that encodes a I-Sce-I site. At best the declaration disclosed chimeric offspring and not transgenic mice) because no germline transmission has been established. Therefore applicant fails to disclose a single transgenic mouse encoding the Group-I intron encoded endonucleases (including I-SceI).

Therefore applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). The applicant fails to disclose all Group-I-intron-encoded endonuclease sites. Furthermore, the transgenic yeast cells, transformed mouse cell lines and/or chimeric offspring, neither represents nor predicts the phenotypic characteristic of transgenic mouse as claimed. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L. P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000). Therefore, the limited disclosure in the specification is not deemed

sufficient to reasonably convey to one skilled in the art that applicants were in possession of a transgenic mouse and/or recombinant cells (as claimed) at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claimed invention.

Claims 53-86 stand rejected under 35 U.S.C. 112, first paragraph, regarding **enablement issues** for the same reasons of record as set forth in the official action mailed on 12/31/01. The applicant argues that transgenic mouse as claimed is predictable and Dr. Choulika's declaration (second) clearly support this assertion (response, pages 5-6). However, this is not found persuasive because Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). The courts have clearly stated that: "A specification did not disclose what is well known in the art. See, e.g., Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F. 2d 1367, 1385, 231 USPQ 81, 94(Fed. Cir. 1986). However, that general off-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific material or of any of the conditions under which a process can be carried out, undue experimentation is required: there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. *It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".* Genentech Inc. V. Novo Nordisk A/s, 42 USPQ2d 1005 (CAFC 1997).

Furthermore, it is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

At best the specification teaches insertion of I-Sce-I site via homologous recombination in mouse NIH3T3 fibroblast and mouse PCC7-s multipotent cell lines using viral vectors (spec. page 64, para.3, page 67, table-1). The specification only exemplified the retroviral infection of a mouse PCC7-s multipotent cell line using viral vectors but fails to disclose that implantation of any selected clone lead to the making of a trasgenic mouse (page 64, para.3, page 67, table-1). Furthermore, the specification teaches genetic recombination, especially the homologous recombination in the making of transgenic yeast (page 3, para.1-2, example 1, 2 and 3). Based upon these results the specification merely speculated that "the method can also be used with transgenic animals" (page 85 para.1, para.3). Similarly, Dr. Choulika's declaration(s) fails to disclose a single transgenic mouse that encodes that encodes the I-Sce-I site. At best the declaration only teaches chimeric offspring wherein the phynotypic expression ranges from 50%-85%. Therefore applicant even fails to disclose a single transgenic mouse encoding the I-SceI recognition site or I-Sce-I endonuclease.

The earlier office action clearly states that the state of transgenic art at the time of filing was such that phenotype of an animal is determined by a complex interaction of genetics and environment. In instant case without sufficient guidance, the genus of transgenic mice encoding any and all Group-I intron endonuclease sites and enddonucleases, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER